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Brief Clinical Report

Familial Arhinia, Choanal Atresia, and Microphthalmia

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We describe two females (aunt and niece) with variable manifestations of arhinia, choanal atresia, microphthalmia, and hypertelorism. In the literature there is only one report on this syndrome in sibs. We hypothesize autosomal dominant inheritance with reduced penetrance.

KEY WORDS: familial arhinia, microphthalmia, choanal atresia

INTRODUCTION

Complete or incomplete absence of nose without other malformations has been reported only in sporadic cases. McKusick [1992, MIM No. 161480] briefly described arhinia in a father and two daughters. There was no mention of ocular or oral malformations. Ruprecht and Majewski [1978] observed arhinia, choanal atresia, microphthalmia, and cleft palate in two daughters of healthy parents. Here, we describe the same anomaly in two generations of one family.

CLINICAL REPORTS

Patient 1 (IV-1)

First daughter (Fig. 1) of healthy, nonconsanguineous parents. Paternity was confirmed by serological examination (99.985%). Birth weight in the 39th week of gestation was 2,620 g, length 50 cm, and OFC 35 cm. There were no postnatal feeding problems, normal statomotor and speech development, no serious illnesses.

Examination at 5 years (Figs. 2, 3) showed: Height 105 cm (10th centile), weight 15 kg, OFC 50.5 cm (90th centile). The forehead was prominent; she also had synophrys, telecanthus (inner canthal distance 42 mm, outer canthal distance 72 mm), short palpebral fissures, blindness due to microphthalmia O.S., and anophthalmia O.D. Stenosis of lacrimal punctae and tear glands present. There was complete absence of nose and nostrils, bilateral preauricular pits, and high palate; also absence of the 12th ribs. Apart from persistent ductus arteriosus, there were no other malformations. Statomotor and mental development was normal. The child is able to hear normally, but it is unclear whether she is able to smell.

Roentgenograms of the skull: hypertelorism, absence of nasal bones, no nasal septum, large single choanal opening, no paranasal sinuses. CT of the skull: No cerebral malformations, the frontal sinuses were underdeveloped, no submucous cleft. CT of the orbits: normal bony orbits and normal olfactory tracts. Chromosomal analysis: Normal karyotype 46,XX (G- and C-banding, 400 band level).

Patient 2 (III-2)

The pregnancy was complicated by hyperemesis and hydramnios, spontaneous birth in the 34th week of gestation, birthweight 1,840 g, length 48 cm (Figs. 4, 5). The baby died after 2 hours. The skull appeared large; there was a slight downward slant of palpebral fissures and hypertelorism. Unfortunately, there is no comment on the eyes. Nasal bones were absent. The rudimentary nose had two dimples instead of nostrils; she had choanal atresia and no paranasal sinuses. Ears were posteriorly angulated with prominent antihelix. She had no cerebral and internal malformations except for partial duplication of the distal vagina. Chromosomes were apparently normal (46,XX, but without banding).

The mother (II-2) of this infant is the grandmother of patient 1. II-2 has a broad nasal tip with a median notch and asymmetrical nostrils. The nasal septum deviated to the right side, but she had no hypertelorism. Diastema between the upper central incisors (Fig. 6). Her daughter (III-1), the 18-year-old mother of patient 1, had synophrys in childhood pictures; now she presents with asymmetrical nostrils, a somewhat broad nasal tip (Fig. 7), and high palate.

DISCUSSION

The malformations of our two patients are similar to those in the sisters described by Ruprecht and Majew-

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Dedicated to Jürgen W. Spranger on the occasion of his 65th birthday with admiration and best wishes.

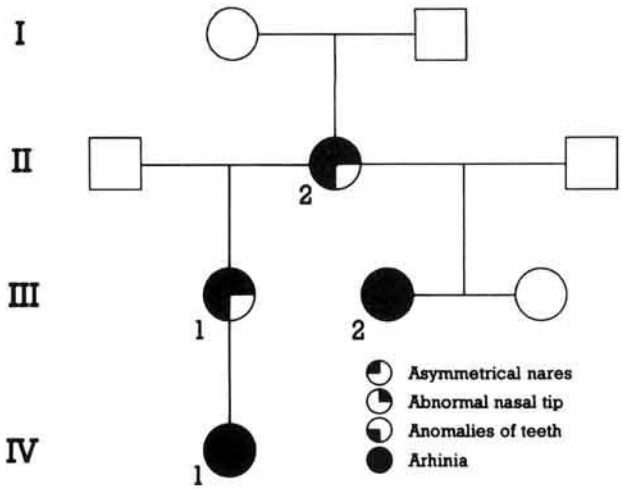

Fig. 1. Pedigree (see text).

Fig. 2. Patient 1, microphthalmia, nasal aplasia.

Fig. 3. Patient 1, high palate.

Fig. 4. Patient 2, tiny nasal tip with two dimples.

Fig. 5. Patient 2, absence of nose.

Fig. 6. II-2, broad and asymmetrical nasal tip, diastema upper central incisors.

Fig. 7. III-1, asymmetrical nostrils, dental anomalies.

ski [1978] (Table I) and include microphthalmia, anophthalmia, absence of nose, and cleft or high palate. The sisters of Ruprecht and Majewski had mild mental retardation. To our knowledge, this syndrome is not yet delineated. All cases of partial or complete absence of the nose described by Gorlin et al. [1990] were sporadic and without further malformations. McKusick [1994, MIM 161480] mentioned absence of nose in a father and two daughters. These cases apparently had no other malformations.

There were no similarities with the different types of frontonasal dysplasia [Cohen et al., 1971; Fuenmayor, 1980]. Absence of nose is caused by a disturbance of the embryonic nasal placodes, whereas frontonasal dysplasia is the consequence of disturbed midface development [Gorlin et al., 1990], causing marked hypertelorism and median cleft face/cleft nose. The common form of frontonasal dysplasia is a sporadic condition [Lorenz et al., 1990]. Craniofrontonasal dysplasia is an autosomal dominant [Kwee and Lindhout, 1988], and faciofrontonasal dysplasia an autosomal recessive trait. There are no similarities between our patients and patients with these disorders.

Ruprecht and Majewski [1978] observed affected sibs born to normal parents. They favored autosomal recessive inheritance as causal explanation. Our famlial observation of the same condition makes dominant inheritance with reduced penetrance likely. Only if patients 1 and 2 had the same father or consanguineous parents is recessive inheritance likely in our family. Both possibilities were denied; the paternity of patient 1 was proven serologically. Affected sibs and normal parents can be explained either by recessive inheritance, germinal mosaicism, or by dominant inheritance with reduced penetrance. The question of whether the mild nasal anomalies of II-2 and III-1 are micromanifestations of this "new" syndrome remains unclear and warrants further study.

TABLE I. Manifestations in Our Two Patients and Two Literature Cases

Findings	Ruprecht/Majewski		Present Patients	
	Patient 1	Patient 2	Patient 1	Patient 2
Arhinia	+	+	+	+
Anosmia	+	+	(+)	?
Hypertelorism	+	+	+	+
Microphthalmia/anophthalmia	+	+	+	?
Cleft/high palate	+	+	+	?
Absence of tear ducts	+	+	+	?
Choanal atresia		+	+	+
Praeauricular fistulas			+	
Patent ductus arteriosus			+	
Absence of 12th ribs			+	
Mental retardation	+	+	–	?
Cerebral malformations	–	–	–	(–)

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